

NON-TECHNICAL ABSTRACT

The overall objective of this study is to perform a clinical trial in colon carcinoma patients comprising immunizations with a mixture of irradiated skin cells genetically modified to express the gene for an immunostimulatory substance, termed IL-2, and irradiated tumor cells. IL-2 gene transfer has resulted in significant anti-tumor immune responses in several animal tumor models. In these studies, the transfer of IL-2 genes into tumor cells has reduced or abrogated tumor formation after implantation into animals. We have successfully induced anti-tumor immunity in an animal model of colorectal carcinoma by immunization with a mixture of irradiated tumor cells and IL-2 transduced skin cells. Immunization with a mixture of irradiated tumor cells and IL-2 modified cells induced anti-tumor immunity capable of rejecting a subsequent live tumor cell challenge. Repeated immunizations with a mixture of irradiated tumor cells and IL-2 modified cells abolished established, visible tumors in a subset of the treated animals. Colorectal carcinoma is one of the most common cancers in the United States and Europe with an annual incidence of greater than 150,000 in the U.S. Most patients are treated with tumor resection and do not have clinically detectable tumor following surgery. However, the majority of patients have microscopic metastases and eventually relapse with clinically overt disease in the liver or abdominal cavity. Encouraging results have been obtained with an autologous tumor vaccine as an additional therapy following tumor resection. Immunization with tumor preparations resulted in a significant increase in disease free and total survival (Hoover et al., J Clin Oncol 11:390, 1993). These findings combined with the demonstration of enhanced anti-tumor immunity following tumor immunizations with cells genetically modified to express IL-2 in several animal tumor systems provide the rationale for using IL-2 gene transfer in our study. Patients will receive immunizations with increasing doses of IL-2 modified skin cells. The patients will be monitored for toxicity, anti-tumor responses and the induction of anti-tumor immunity. The results of the Phase I trial should permit an assessment of the safety of this form of gene transfer and provide initial data to evaluate the potential utility of IL-2 gene therapy with a mixture of genetically modified skin cells and irradiated tumor cells.